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EXAMINER: TUSCAN, M
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DATE MAILED: 06/07/94

This is a communication from the examiner in charge of your application.
COMMISSIONER OF PATENTS AND TRADEMARKS

☒ This application has been examined ☒ Responsive to communication filed on Feb 9, 1994 ☒ This action is made final.

A shortened statutory period for response to this action is set to expire 3 month(s), ___ days from the date of this letter.
Failure to respond within the period for response will cause the application to become abandoned. 35 U.S.C. 133

Part I THE FOLLOWING ATTACHMENT(S) ARE PART OF THIS ACTION:

1. ☒ Notice of References Cited by Examiner, PTO-892.
2. ☐ Notice of Draftsman's Patent Drawing Review, PTO-948.
3. ☐ Notice of Art Cited by Applicant, PTO-1449.
4. ☐ Notice of Informal Patent Application, PTO-152.
5. ☐ Information on How to Effect Drawing Changes, PTO-1474.
6. ☐ _____.

Part II SUMMARY OF ACTION

1. ☒ Claims 23, 26-33 are pending in the application.
   Of the above, claims 26-31 are withdrawn from consideration.
2. ☐ Claims 24&25 have been cancelled.
3. ☐ Claims _____ are allowed.
4. ☒ Claims 23, 32-33 are rejected.
5. ☐ Claims _____ are objected to.
6. ☐ Claims _____ are subject to restriction or election requirement.
7. ☐ This application has been filed with informal drawings under 37 C.F.R. 1.85 which are acceptable for examination purposes.
8. ☐ Formal drawings are required in response to this Office action.
9. ☐ The corrected or substitute drawings have been received on _____. Under 37 C.F.R. 1.84 these drawings are ☐ acceptable; ☐ not acceptable (see explanation or Notice of Draftsman's Patent Drawing Review, PTO-948).
10. ☐ The proposed additional or substitute sheet(s) of drawings, filed on _____, has (have) been ☐ approved by the examiner; ☐ disapproved by the examiner (see explanation).
11. ☐ The proposed drawing correction, filed _____, has been ☐ approved; ☐ disapproved (see explanation).
12. ☐ Acknowledgement is made of the claim for priority under 35 U.S.C. 119. The certified copy has ☐ been received ☐ not been received ☐ been filed in parent application, serial no. _____; filed on _____.
13. ☐ Since this application apppears to be in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under Ex parte Quayle, 1935 C.D. 11; 453 O.G. 213.
14. ☐ Other

EXAMINER'S ACTION

PTOL-326 (Rev. 2/93)

16. The amendment dated February 9, 1993 has been received and made of record. Claims 23 and 26-33 are pending. Claims 24 and 25 have been cancelled. Claims 26-31 are withdrawn from further consideration by the Examiner, 37 C.F.R. § 1.142(b) as being drawn to a nonelected invention. Election was made **without** traverse in Paper No. 5. Accordingly, claims 23 and 32-33 are under examination.

17. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

18. The rejection of claim 23 under 35 U.S.C. § 101 as lacking patentable utility has been withdrawn in light of the amendment to claims 23 adding a recovery step for the antibodies, i.e. the claim no longer reads on a method of vaccination or inducing protective immunity.

19. The rejection of claims 23 and new claims 32-33 under 35 U.S.C. § 112, first paragraph as the specification does not provide support for the invention as now claimed is maintained for the reasons of record in the previous office action.

Applicants argue that the techniques of producing antibodies were well known in the art at the time of the invention and that the information need not to be described in the specification to enable the claimed invention.

These arguments have been carefully considered, but after careful review of the as-filed specification, are not found to be

persuasive. As set forth in the previous office action, the specification fails to set forth a methods of producing or raising antibodies with the recited steps, i.e. providing the expression product, raising the antibodies and recovering said antibodies. See page 13 for the contemplated uses of the λ-J19 clone, including the transfection of the DNA into host cells, the expression of protein encoded by the DNA, the production of fusion peptides, the synthesis of oligonucleotide, and vaccine compositions. No where in the specification is a method with claimed step of recovering antibodies set forth. Accordingly, the as-filed specification provides no evidence of conception of the invention as now claimed.

As to applicants' argument that the methods of producing antibodies are so well known that they need not be included in the specification, applicants are directed to the essential steps of the claimed methods. The specification teaches only the isolation and rough restriction map of the J-19 clone. The specification fails to provide evidence that any single step of the claimed method was reduced to practice at the time of filing. Step (a) of the instant claims requires "providing an antigen of HIV-1, wherein said antigen is the expression product of a host transformed..." The specification fails to teach the identity of any encoded antigen, does not teach the location of any open reading frame contained within the clone, does not teach the sequence of the DNA that would enable the skilled artisan to

locate **potential** open reading frames, and does not teach the expression of any single antigen. Even if the skilled artisan possessed knowledge as to the open reading frames contained within the J-19 clone, the successful expression of a protein in an antigenically relevant form is often problematic. As an example, Kamtekar et al. addresses some of the problems associated with the over-expression of heterologous proteins that still plagued researchers in 1993. Kamtekar et al. state that "overexpression of many natural proteins has been hindered by difficulties with folding, stability, or solubility" and further recites two of the common outcomes of overexpression. These outcomes include no expression and expression wherein the protein forms insoluble inclusion bodies (see paragraph spanning pages 1682-1683. Accordingly, the specification does not enable even the first step of the instant claims, i.e. "providing an antigen of HIV-1".

The cited references (Exhibits 1-3) merely teach the general methods of raising antibodies and producing monoclonal antibodies. The references do not teach how to arrive with the first step of the claimed methods, i.e. providing the instant antigen. It is also noted that these references are not cited in the specification as exemplifying the well known methods of antibody production. The decision set forth in *In re Strahiletz* is not applicable to the lack of teachings of the instant specification as the specification completely lacks a written

description of the claimed methods. Accordingly, the specification provides no evidence that applicants even contemplated the method as is now claimed at the time of filing.

20. The rejection of claim 23 and new claims 32 and 33 under 35 U.S.C. 102(b) as being anticipated by any one of Robey et al. (1986), Rusche et al. (1987), Lasky et al. (1986), Chanh et al. (1986) or Putney et al. (1986) is maintained for the reasons of record reiterated below.

Robey et al. disclose a method of producing antibodies to LAV by raising antibodies against gp120 (see p.7024, under Immunization with gp120). See also Fig.3, wherein the reactivity of the induced antibodies is demonstrated by the ability of the antibodies to immunoprecipitate labelled gp120. i.e. the antibodies produced were recovered.

Rusche et al. disclose a method of producing antibodies against LAV by raising antibodies against recombinant gp160 (see p.6926, third full paragraph), These antibodies effectively neutralized in vivo viral infection (see Fig.5), i.e. the antibodies were recovered.

Lasky et al. disclose a method of producing antibodies against LAV by raising antibodies against a truncated form of the envelope protein (see p.211, top of page). In this case, goats are immunized with the protein formulated with Freund's complete adjuvant.

Chanh et al. disclose a method of producing antibodies against LAV by raising antibodies against of a envelope peptide (see p.3069, last paragraph).

Putney et al. disclose a method of producing antibodies against LAV by raising antibodies against the carboxyl-terminal 180 amino acids of gp120 (see p.1393, middle column, first full paragraph).

As the specification teaches that the DNA fragment of clone J19 with the restriction sites set forth in claims 23-25 encodes the envelope protein, the limitations of the above claims are fully met by any one of these prior art references.

Note that all of the above references include a characterization step for the antibodies induced, i.e. the antibodies are recovered.

Applicants argue that none of the above references are available as prior art as the claimed priority date for the instant claims is that of the British application, i.e. September 19, 1984. This argument has been carefully considered but is found unpersuasive for the reasons set forth above, i.e. the specification does not provide support for the invention as now claimed. Accordingly, the priority date awarded to the claims 23 and 32-33 is that of instant application and the above rejection under 35 U.S.C. § 102(b) is maintained.

21. No claims are allowed.

22. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 C.F.R. § 1.136(a).

A SHORTENED STATUTORY PERIOD FOR RESPONSE TO THIS FINAL ACTION IS SET TO EXPIRE THREE MONTHS FROM THE DATE OF THIS ACTION. IN THE EVENT A FIRST RESPONSE IS FILED WITHIN TWO MONTHS OF THE MAILING DATE OF THIS FINAL ACTION AND THE ADVISORY ACTION IS NOT MAILED UNTIL AFTER THE END OF THE THREE-MONTH SHORTENED STATUTORY PERIOD, THEN THE SHORTENED STATUTORY PERIOD WILL EXPIRE ON THE DATE THE ADVISORY ACTION IS MAILED, AND ANY EXTENSION FEE PURSUANT TO 37 C.F.R. § 1.136(a) WILL BE CALCULATED FROM THE MAILING DATE OF THE ADVISORY ACTION. IN NO EVENT WILL THE STATUTORY PERIOD FOR RESPONSE EXPIRE LATER THAN SIX MONTHS FROM THE DATE OF THIS FINAL ACTION.

23. Papers related to this application may be submitted to Group 180 by facsimile transmission. Papers should be faxed to Group 180 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center Telephone Numbers are (703) 308-4227 and (703) 305-3014.

24. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Examiner Tuscan whose telephone number is (703) 308-4240.

CHRISTINE M. NUCKER
SUPERVISORY PATENT EXAMINER
GROUP 180

Michael S. Tuscan, Ph.D.
June 1, 1994